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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,244	12/27/2001	David Botstein	P2930R1C2	1015

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 09/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	10/033,244	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 8/23/2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: 22-27.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☒ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). 4/21/03 & 4/29/03

10. ☐ Other: _____

Jeffrey Fredman
Primary Examiner
Art Unit: 1637

8/31/04

Continuation of 5. does NOT place the application in condition for allowance because: The Declarations are fundamentally flawed because they fail to provide specific evidence regarding Pro-1800. Each Declaration, the Polakis Declaration, the Goddard Declaration, the Grimaldi Declaration and the Ashkenazi Declaration state that, generically, increased mRNA levels may predict increased protein levels. However, besides the three references cited in the rejection, the declarations themselves support the position that the increase is not necessarily correlative. In the Polakis declaration, the Declarant notes at page 2 that about 80% of the mRNAs had expression levels which correlate with the expression level of the proteins, meaning that in this sample, 20% did of the mRNAs had expression levels which did NOT correlate with the protein expression levels.
So each Declaration represents solely the opinion of the Declarant regarding proteins in general, not Pro-539 in particular. There is no specific declaration which states that Pro-1800 is overexpressed. There is no evidence of record that Pro-539 is overexpressed. There is significant evidence cited in the rejection, and found in the Declarations, that it is not inherent that mRNA overexpression yields protein overexpression. This is the factual conclusion which may be drawn from these declarations

Applicant then argues the legal conclusion of lack of utility based upon the factual predicate discussed above in the response to declarations that while there can be a relationship between mRNA and protein expression, it is not inherent that mRNA overexpression yields protein overexpression
So when Applicant makes the statement that "The general, accepted understanding in the art is that the level of protein expression would therefore also be increased," this statement represents mere supposition. There is no evidence to support this specific assertion with regard to Pro-1800. The Polakis declaration itself demonstrates that at least 20% of the time, using the samples of Applicant, this would not be true.
Further, there is no necessary expectation that the tumors or samples of Applicant are representative. As the cited prior art of Meric and Gokman-Polar make clear, it is not a predictable element whether increased mRNA levels yield increased protein expression levels.
In analyzing utility, the first place to begin is with the decision of the Supreme Court in Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). In Brenner, the Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.
There is no specific benefit, in currently available form, for the Pro-1800 protein and antibody, since there are no specific and substantial utilities for that Pro-1800 protein and antibody.
The CCPA first applied Brenner in In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are-or are not-in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.
The current situation is identical to that in Kirk. The Declarations filed provide evidence that one could determine whether the Pro-539 protein is useful, but do not even show any utility specifically for Pro-539 as discussed above. Further, the discussion cited by Applicant of the various declarations, such as the discussion on page 16 of the response, clearly represent language which is "useful in research" but has no current practical use. The speculation by the Declarants that medical practitioners might wish to know if proteins in general are overexpressed, without reference to Pro-539 in particular, is precisely the sort of vague argument which lacks any specificity.
There is no particular therapy associated with overexpression of the Pro-539 protein. There is no particular diagnosis associated with overexpression of the Pro-1800 protein. There is no particular use whatsoever associated with overexpression of the Pro-1800 protein and resultant antibody. There are only vague general statements that such an overexpression might be useful in research or therapy. This is insufficient according the to the Kirk court.

This is particularly demonstrated when Applicant argues that the proteins might be useful for tissue typing (see page 17). This is a classic throwaway utility since there is no evidence that Pro-1800 protein is associated with any particular tissue at all.

Similarly, with regard to specific utility, the declaration, the arguments and the specification are entirely silent on any real specific utility for Pro-1800. When Applicant states that evidence of overexpression of PRO1800 nucleic acids provides utility to the protein, this presumes the protein is similarly overexpressed. As discussed at length above, this is not necessarily the case. Consequently, this cannot serve as a foundation stone to support specific utility.

Since Applicant's underlying arguments are not found persuasive for the reasons given above, the conclusion necessarily differs. For the reasons given above, the current claims lack specific and substantial utility.

With regard to enablement, fundamentally the same arguments apply, and this rejection is maintained for the same reasons as given above in response to the arguments on utility..